Claims

We claim:

1. Lymphotoxin-ß, a lymphocyte membrane-type polypeptide comprising SEQ ID NO:2.

2. The polypeptide according to claim 1 wherein the polypeptide is associated with a cell surface.

3. The polypeptide according to claim 2 wherein the polypeptide is associated with the surface of OKT3-stimulated primary T cells, antigen-specific IL-2 dependent CTL clones, and a PMA-stimulated human T cell hybridoma, II-23.D7.

4. A soluble lymphotoxin-ß peptide comprising an amino acid sequence selected from the group consisting of:

(a) SEQ ID NO:4;

(b) SEQ ID NO:6; and

(c) an amino acid sequence represented by the following formula:

X - SEQ ID NO:6,

wherein X comprises one or more of the amino acid residues starting from the 3' end of SEQ ID NO:8.

5. A peptide according to claim 4 further comprising a leader sequence at the 5' end.

6. A polypeptide comprising an amino acid sequence that is encoded by a DNA from the group consisting of:

(a) a DNA sequence comprising SEQ ID NO:1;

(b) DNA sequences that hybridize to the DNA defined by SEQ ID NO:1 and that code on expression for a polypeptide that is substantially homologous with lymphotoxin-ß; and

(c) DNA comprising degenerate nucleotide sequences that code for the polypeptide that is encoded by the DNA sequence defined by SEQ ID NO:1.

7. A polypeptide comprising an amino acid sequence that is encoded by a DNA from the group consisting of:

(a) a DNA sequence comprising SEQ ID NO:3;

(b) a DNA sequence comprising SEQ ID NO:5;

(c) a DNA sequence represented by the following formula:

X - SEQ ID NO:5,

wherein X comprises one or more of the nucleoside triplets starting from the 3' end of SEQ ID NO:7;

(d) DNA sequences that hybridize to any one of SEQ ID NO:3, SEQ ID NO:5 and the sequence according to part (c) above and that code on expression for a polypeptide that is substantially homologous with a soluble lymphotoxin-ß peptide; and

(e) a DNA sequence comprising degenerate nucleotide sequences that code for the polypeptide encoded for any one of SEQ ID NO:3, SEQ ID NO:5 and the sequence according to part (c) above.

8. An engineered polypeptide comprising the amino acid sequence defined by SEQ ID NO:2 wherein the sequence Leu Gly Leu is cleaved from the 5' end of said sequence and replaced by a single Met or Leu residue.

9. An isolated DNA sequence selected from the group consisting of:

(a) a DNA sequence comprising the nucleotide sequence defined by SEQ ID NO:1;

(b) a DNA sequence that hybridizes with the DNA sequence defined by SEQ ID NO:1 and that codes on expression for a polypeptide that is substantially homologous with lymphotoxin-ß; and

(c) a DNA sequence comprising degenerate nucleotide sequences that code for lymphotoxin-ß.

10. An isolated DNA sequence selected from the group consisting of:

(a) a DNA sequence comprising the nucleotide sequence defined by SEQ ID NO:3;

(b) a DNA sequence comprising the nucleotide sequence defined by SEQ ID NO:5;

(c) a DNA sequence comprising the nucleotide sequence according to claim 7(c);

(d) DNA sequences that hybridize to a DNA sequence as defined by any one of SEQ ID NO:3, SEQ ID NO:5 or the sequence according to claim 7(c) and that code on expression for a polypeptide that is substantially homologous with a soluble lymphotoxin-ß peptide; and

(e) a DNA sequence comprising degenerate nucleotide sequences that code for a soluble lymphotoxin-ß peptide.

11. An engineered DNA sequence comprising the nucleotide sequence defined by SEQ ID NO:1 wherein the nucleotides CTGGGGCTG are cleaved from the 5' end of said sequence and replaced by a single start codon.

12. A recombinant DNA molecule comprising a DNA sequence selected from the group consisting of:

(a) a DNA sequence defined by SEQ ID NO:1;

(b) a DNA sequence defined by SEQ ID NO:3;

(c) a DNA sequence defined by SEQ ID NO:5;

(d) a DNA sequence according to claim 7(c);

(e) a DNA sequence according to Claim 11;

(f) a DNA sequence that hybridizes with the DNA sequences defined by any one of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 and the sequence according to claim 7(c) and that codes on expression for lymphotoxin-ß or a soluble lymphotoxin-ß peptide;

(g) a DNA sequence comprising degenerate nucleotide sequences that codes for lymphotoxin-ß; and

(h) a DNA sequence comprising degenerate nucleotide sequences that codes for a soluble lymphotoxin-ß peptide.

13. A host selected from the group consisting of unicellular hosts, animal cells in culture and human cells in culture, transfected with the recombinant DNA molecule of claim 12.

14. The host according to claim 13 selected from the group of tumor infiltrating lymphocytes, lymphokine activated killer cells, killer cells and genetically engineered tumor cells removed from a patient.

15. A method for producing the polypeptide of any one of claims 1 to 8, said method comprising the steps of culturing a transformed host according to claim 13 and collecting the polypeptide.

16. A polypeptide complex comprising a first polypeptide selected from a group consisting of the amino acid sequence defined by any one of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, a polypeptide according to claim 8, and soluble lymphotoxin-ß peptide according to claim 4(c), and a second polypeptide selected from the group consisting of lymphotoxin-α, native human or animal lymphotoxin, recombinant lymphotoxin, soluble lymphotoxin, secreted lymphotoxin, or lymphotoxin or lymphotoxin-active fragments of any of the above.

17. A polypeptide complex comprising a plurality of lymphotoxin-ß polypeptide units.

18. A polypeptide complex according to claim 16 wherein the complex is associated with a cell surface.

19. A polypeptide complex according to claim 18 wherein the first polypeptide is associated with the surface of OKT3-stimulated primary T cells, antigen-specific IL-2 dependent CTL clones, and a PMA-stimulated non-lymphotoxin human T cell hybridoma, II-23.D7.

20. A method for producing lymphotoxin epitopes on the surface of a cell comprising the steps of transfecting the cell with a recombinant DNA molecule according to claim 12 and expressing that DNA in the cell.

21. A method for enhancing the targeting tumorcidal activity of tumor infiltrating lymphocytes comprising the steps of transfecting the lymphocytes with a recombinant DNA molecule according to claim 12 and introducing the transformed lymphocytes to a patient.

22. The method according to claim 21, wherein the transformed lymphocytes are incubated with a lymphokine before or after transfection with the recombinant DNA molecule according to claim 12.

23. The method according to claim 22, wherein the lymphokine is IL-2.

24. A composition for preventing, treating or lessening the advancement, severity or effects of HIV infection, neoplasia, inflammation or inflammatory disease, or autoimmune disease comprising an effective amount of a polypeptide selected from the group consisting of a polypeptide according to any one of claims 1 to 8, a polypeptide

complex according to any one of claims 16-19, antibodies to any one of the above, or a combination of any of the above, and a pharmaceutically acceptable carrier.

25. A method for preventing, treating or lessening the advancement, severity or effects of HIV infection, neoplasia, inflammation or inflammatory diseases, or autoimmune disease comprising administering an effective amount of a polypeptide selected from the group consisting of a polypeptide according to any one of claims 1-8, a polypeptide complex according to any one of claims 16-19, antibodies to any one of the above, or a combination of any of the above, and a pharmaceutically acceptable carrier.

26. A composition for suppressing the immune system comprising an effective amount of a polypeptide selected from the group consisting of a polypeptide according to any one of claims 1 to 8, a polypeptide complex according to any one of claims 16-19, antibodies to any one of the above, or a combination of any of the above, and a pharmaceutically acceptable carrier.

27. A method for suppressing the immune system comprising administering an effective amount of a polypeptide selected from the group consisting of a polypeptide according to any one of claims 1-8, a polypeptide complex according to any one of claims 16-19, antibodies to any one of the above, or a combination of any of the above, and a pharmaceutically acceptable carrier.

28. A nucleotide sequence coding for lymphotoxin-ß comprising the nucleotide sequence represented by SEQ ID NO:1 and further comprising an engineered nucleotide sequence at the 5' end wherein said engineered sequence comprises a functional start codon that is either ATG or CTG and wherein any other codon within said engineered sequence coding for leucine is not CTG.